CLAIMS

We claim:

1. A targeting construct comprising:

(a) a first polynucleotide sequence homologous to a melanocortin-3 receptor gene;

(b) a second polynucleotide sequence homologous to the melanocortin-3 receptor gene; and

(c) a selectable marker.

2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.

3. A method of producing a targeting construct, the method comprising:

(a) providing a first polynucleotide sequence homologous to a melanocortin-3 receptor gene;

(b) providing a second polynucleotide sequence homologous to the melanocortin-3 receptor;

(c) providing a selectable marker; and

(d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.

4. A method of producing a targeting construct, the method comprising:

(a) providing a polynucleotide comprising a first sequence homologous to a first region of a melanocortin-3 receptor gene and a second sequence homologous to a second region of a melanocortin-3 receptor gene;

(b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.

5. A cell comprising a disruption in a melanocortin-3 receptor gene.

6. The cell of claim 5, wherein the cell is a murine cell.

7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.

8. A non-human transgenic animal comprising a disruption in a melanocortin-3 receptor gene.

9. A cell derived from the non-human transgenic animal of claim 8.

10. A method of producing a transgenic mouse comprising a disruption in a melanocortin-3 receptor gene, the method comprising:

(a) introducing the targeting construct of claim 1 into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a melanocortin-3 receptor, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a melanocortin-3 receptor gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression of melanocortin-3 receptor in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a melanocortin-3 receptor, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a melanocortin-3 receptor gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the function of the disrupted melanocortin-3 receptor gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of melanocortin-3 receptor, the method comprising:

(a) providing a cell comprising a disruption in a melanocortin-3 receptor gene;

(b) contacting the cell with an agent; and

(c) determining whether expression of the melanocortin-3 receptor is modulated.

14. A method of identifying an agent that modulates the function of a melanocortin-3 receptor gene, the method comprising:

(a) providing a cell comprising a disruption in a melanocortin-3 receptor gene;

(b) contacting the cell with an agent; and

(c) determining whether the function of the melanocortin-3 receptor gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a melanocortin-3 receptor gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a kidney abnormality or a behavioral abnormality.

18. The transgenic mouse of claim 17, wherein the kidney abnormality is absence of one kidney.

19. The transgenic mouse of claim 17, wherein the kidney abnormality is reduced size of the kidney relative to a wild-type mouse.

20. The transgenic mouse of claim 17, wherein the kidney comprises unilateral renal agenesis.

21. The transgenic mouse of claim 17, wherein the behavioral abnormality is passivity.

22. The transgenic mouse of claim 17, wherein the behavioral abnormality is hypoactivity.

23. The transgenic mouse of claim 17, wherein the behavioral abnormality is decreased locomotion.

24. The transgenic mouse of claim 17, wherein the behavioral abnormality is a decrease in the attempt to escape while being examined relative to a wild type mouse.

25. The transgenic mouse of claim 17, wherein the behavioral abnormality is absence of any attempt to escape while being examined.

26. The transgenic mouse of claim 17, wherein the behavioral abnormality is observed in males.

27. A method of producing a transgenic mouse comprising a disruption in a melanocortin-3 receptor gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a kidney abnormality or a behavioral abnormality, the method comprising:

(a) introducing a melanocortin-3 receptor gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a melanocortin-3 receptor gene.

28. A transgenic mouse produced by the method of claim 27.

29. A cell derived from the transgenic mouse of claim 17 or claim 28.

30. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a melanocortin-3 receptor gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a melanocortin-3 receptor gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: a kidney abnormality or a behavioral abnormality.

31. A method of identifying an agent that modulates melanocortin-3 receptor expression, the method comprising:

(a) administering an agent to the transgenic mouse comprising a disruption in a melanocortin-3 receptor gene; and

(b) determining whether the agent modulates melanocortin-3 receptor expression in the transgenic mouse, wherein the agent has an effect on at least one of the following behaviors: passivity, locomotion or attempts to escape while being examined.

32. A method of identifying an agent that modulates a behavior associated with a disruption in a melanocortin-3 receptor gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a melanocortin-3 receptor gene; and

(b) determining whether the agent modulates passivity, locomotion or attempts to escape while being examined.

33. A method of identifying an agent that modulates melanocortin-3 receptor gene function, the method comprising:

(a) providing a cell comprising a disruption in a melanocortin-3 receptor gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates melanocortin-3 receptor gene

function, wherein the agent modulates a phenotype associated with a disruption in a melanocortin-3 receptor gene.

34. The method of claim 33, wherein the phenotype comprises at least one of the following: a kidney abnormality or a behavioral abnormality.

35. An agent identified by the method of claim 30, claim 31, claim 32, or claim 33.

36. An agonist or antagonist of a melanocortin-3 receptor.

37. Phenotypic data associated with the transgenic mouse of claim 17 or claim 28, wherein the data is in a database.